Impact of Post-Antibiotic Effect Induced by Clindamycin and Chlorhexidine on the Virulence Factors of Oral Streptococci and Staphylococci

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INTRODUCTION

The post-antibiotic effect (PAE) appears to be a phenomenon that represents a suppression of bacterial growth after exposure to antibiotic for a specific period. The period of growth suppression is related to the target site of antibiotic as well as the type of microorganisms. Thus protein synthesis inhibitors are usually prolonged PAE period especially against gram-positive bacteria. While cell wall synthesis inhibitors are usually induced short or even no PAE period against gram-negative bacteria (Rayner and Munckhof, 2005 & Hanberger *et al*., 1991).

Several factors affecting the presence and/or the duration of PAE these factors are: (i) Type of microorganism (ii) Type of antimicrobial agent and its concentration (iii) Exposure time and (iv) Antimicrobial combination.

Other factors affecting duration of PAE such as: (i) Temperature; (ii) Oxygen level; (iii) Growth medium; and (iv) pH of the medium. The duration of PAE is varied according to the type of antibiotic as well as the type of the organism , Thus protein synthesis inhibitors are usually produced longer period against gram-positive bacteria.

Exposure of oral ***Staphylococcus aureus*** and ***Streptococcus mutans*** to a clindamycin at a concentration of one µg/ml For 1 hour induced long PAE period. This period seems that it is a concentration dependent with most of antibiotics.

Actually clindamycin showed a considerable and concentration dependent PAEs against gram-positive cocci, especially streptococci and staphylococci (Drinkovic *et al*., 2001).

The importance of PAE as a pharmacodynamic parameter is primary related to its potential influence on antimicrobial dosing regimen in clinical practice. Agent inducing a long PAE may be administered with longer dosing intervals without loss of efficacy. This integrates the microbiological and pharmacokinetics properties of antibiotics to predict the best dosage schedules that will provide maximal efficacy and minimal toxicity.

Clindamycine is commonly used systematically in the treatment of oral infectious diseases and other diseases, resulted from infection with anaerobic and gram-positive infections. This antibiotic is commonly used systematically in combination with chlorhexidine, in the form of mouthwash (Rask *et al*., 1988).

Therefore, the study was conducted to determine the PAE induced by clindamycine and/or chlorhexidine against oral streptococci and staphylococci. The study was focused on the physiological changes that are occurred during and after PAE period.

Such changes represent the main virulence factors of staphylococci and streptococci, namely: cell morphology; cell adherence; enzyme production and toxin productions.

The following methodologies will be carried out to achieve the above objectives; including:

i. Isolation of streptococcus and staphylococcus species from clinical specimens

ii. Determination of susceptibilities of the recovered isolates against clindamycin and/or chlorhexidine, by determination of MICs (minimum inhibitory concentration) for the recovered isolates, according to the method recommended by NCCLS (2004)

iii. Determination of PAE period by determination of the changes in the viable counts, and/or spectrophotometric technique for growth turbidity, before and after removal of the antibiotic

iv. Determination of physiological changes in: (I) cell morphology, (II) cell adherence), (III) enzyme production and (IV) hemolysin production before and after PAE period.

1. Literature Review

1.1. History of Post-antibiotic Effect:

The post-antibiotic effect (PAE) is the term used to describe suppression of bacterial growth that persists after brief exposure of organisms to antimicrobial agent (Spangler *et al*., 1998). In 1944, Bigger noted delayed development in turbidity after adding penicillinase to culture of staphylococci previously exposed to penicillin G. after few years Parker and Luse, (1948) and Parker and Marsh, (1946) noticed that staphylococci shortly exposed to penicillin and transferred to a drug free medium did not resume normal growth for up to three hours. Other investigator like Eagle and co-workers confirmed and extended these observations with penicillin to staphylococci and streptococci both *in-vitro* and *in-vivo* (Eagle *et al.,* 1950 & Eagle and Musselman, 1949).

It was observed that most antimycobacterial drugs induced an extended bacterial lag of regrowth (Mitchinson and Dickinson, 1971). However, it is not until the mid-1970s that these initial observations on the PAE were applied to gram-negative bacteria and antimicrobials developed after penicillin (McDonald *et al*., 1977; Rolinson *et al*., 1977). Thus, during the past two decades, PAE has been proved in almost every bacteria-drug combination tested.